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PATENT COOPERATION TREATY PCT/PTO 30 NOV 2004

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 02008283.0	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/04103	International filing date *(day/month/year)* 17.04.2003	Priority date *(day/month/year)* 22.04.2002
International Patent Classification (IPC) or both national classification and IPC A61K47/48		
Applicant BIOMAY PRODUKTIONS- UND HANDELS-AKTIEN..., et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.11.2003	14.05.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Steinheimer-Breitkre Telephone No. +49 89 2399-7115

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/04103

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-16 as originally filed

Claims, Numbers

1-12 received on 01.04.2004 with letter of 31.03.2004

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 9-10

   because:

   ☒ the said international application, or the said claims Nos. 9-10 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-12
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-8,11-12
	No:	Claims	

2. Citations and explanations

see separate sheet

III Non-establishment of report

Claims 9-10 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability

V.1 Documents cited

Reference is made to the following documents:

D1: WO84-00294

D2: US-A-5 849 884 (BROWN LARRY R ET AL) 15 December 1998 (1998-12-15)

D3: GEETA N SAI ET AL: 'In vitro immunization of murine lymphocytes using immobilized immunogens.' BIOTECHNOLOGY AND APPLIED BIOCHEMISTRY, vol. 24, no. 1, 1996, pages 61-64, XP008009290 ISSN: 0885-4513

D4: WO 95 19437 A (MOHAPATRA SHYAM S ;UNIV MANITOBA (CA); SEHON ALEC H (CA)) 20 July 1995 (1995-07-20)

D5: EP-A-0 451 800 (ABBOTT LAB) 16 October 1991 (1991-10-16)

D6: SCHRAMM G ET AL: "Allergen engineering': variants of the timothy grass pollen allergen Phl p 5b with reduced IgE-binding capacity but conserved T cell reactivity.' JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) UNITED STATES 15 FEB 1999, vol. 162, no. 4, 15 February 1999 (1999-02-15), pages 2406-2414, XP002216586 ISSN: 0022-1767

Document D1 was not cited in the International Search Report and is cited in view of the PCT Guidelines VI-7.24. A copy of the document is annexed to this report.

V.2 Novelty, Inventive Step and Industrial Applicability (Art. 33 PCT)

2.1 The prior art as represented by D1-D6 is silent as to the following features:
The use of timothy grass pollen or other plant pollen as allergen in a microparticle comprising a bead consisting of cross-linked carbohydrate and covalently bound

allergen. **The subject-matter of claims 1-12 therefore appears to be novel.**

2.2 D1 describes microparticles comprising a bead consisting of cross-linked carbohydrate (e.g. agarose, p. 4-5 and claim 4) and an allergen (p. 12) that is covalently bound to the bead (claim 1 of D1). The microparticle is used for vaccination (p. 2-3) or treatment of allergies, for instance (p. 12).
The present application is different from D1 in that the allergen is derived from plant pollen. and that the bead consists of threedimensionally cross-linked carbohydrate.

According to the applicants explanations, the covalent binding of the allergen to a bead that essentially consists of threedimensionally cross-linked carbohydrate prevents that the allergen is released from the bead.

The technical effect is therefore that allergen preparations with allergen derived from plant pollen are provided in a form which does not allow the allergen to be released from the bead, which would enhance the risk that the patient suffers from an anaphylactic shock.

The problem of the invention can therefore be regarded as providing microbeads with plant allergen whereby the allergen cannot be released from the beads.

D4-D6 disclose the use of pollen as allergens, especially timothy grass pollen (D4: p. 7; D5; p. 8; D6: p. 2406). D4 also discloses polymer-linked allergen (p. 9), using different polymers. The problem that the allergen might be released from the beads, which should be avoided, is nowhere mentioned in D4-D6.
D1 discusses the covalently coupling of the substrate to the matrix, but stresses that in this case the technique of covalent coupling should not imply any appreciable degree of cross-linking of the matrix, because such cross-linking would completely annihilate the release mechanisms (p. 7, l. 18-26), which are essential to the beads of D1. D1 thus teaches away from the present invention.
Thus, the subject-matter of claims 1-12 does involve an inventive step and does satisfy the criterion set forth in Article 33(3) PCT.

2.3 For the assessment of the present claims 9-10 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO,

for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

All other claims are considered to be industrially applicable.

V.3 The Applicant should also consider the following objections:

3.1 Claims 7 and 8 concern beads that are suitable for specific medical applications. The claims do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved (i.e. being suitable for certain applications) which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result are missing.

3.2 The term "essentially" used in claims 1 and 2 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

3.3 Contrary to the requirements of Rule 5.1 (a)(ii) PCT, the relevant background art disclosed in the documents D1-D6 is not mentioned in the description, nor are these documents identified therein.

PCT/EP03/04103
Biomay Produktions- und Handels-Aktiengesellschaft et al.

CLAIMS

1. Microparticle comprising

a) a bead essentially consisting of a threedimensionally cross-linked carbohydrate and
b) an allergen which is covalently bound to the bead, wherein
c) the allergen is derived from plant pollen.

2. Microparticle according to claim 1 wherein the carbohydrate bead consists essentially of agarose.

3. Microparticle according to claim 1 wherein the allergen is derived from grass pollen.

4. Microparticle according to claim 3 wherein the allergen is derived from timothy grass pollen.

5. Microparticle according to any one of claims 1-4 wherein the particle size ranges from 0.1 µm to 10 µm.

6. Microparticle according to any of claims 1-5 wherein the particle size ranges from 0.5 µm to 5 µm.

7. Microparticle according to any of claims 1-6 characterized in that the microparticle is used for vaccination.

8. Microparticle according to any of claims 1-7 characterized in that the microparticle is used for the treatment of allergy.

9. Medicament for the treatment of the immune system characterized in that it comprises microparticles according to any of claims 1-8.

10. Medicament according to claim 9 characterized in that it is prepared for parenteral application.

11. Diagnostic test system for the measurement of released cell mediators characterized in that is comprises microparticles according to any of claims 1-6.

12. Diagnostic test system according to claim 11 wherein the released cell mediator to be measured is an interleukin.